Management of ICP elevation

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Topics to cover

- ICP: normal and abnormal
- ICP Measurement tools
  - Invasive (parenchymal vs. global ventricular)
  - Non-invasive (TCD related, ONSD)
- ICP: waveform for brain compliance
- Stepwise approach to ICP control
  - Pros and cons for each step

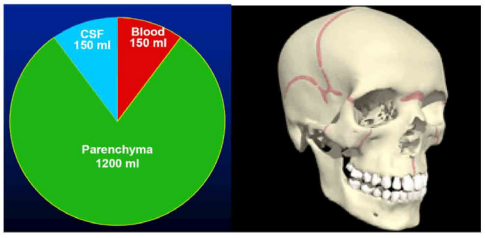
1. Intracranial pressure

Table 1 Normal intracranial pressure values

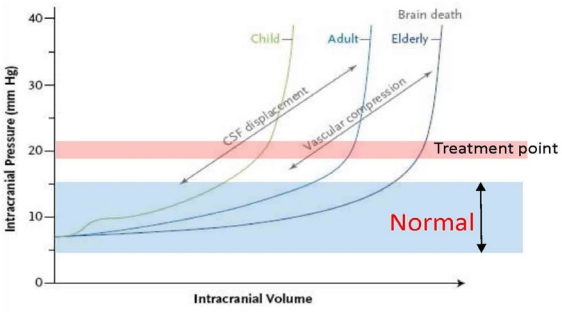
Age group	Normal range (mm Hg)
Adults	<10–15
Children	3–7
Term infants	1.5–6

J Neurol Neurosurg Psychiatry 2002

1mm Hg = 1.36 cm H_2O



Monro-Kellie principle

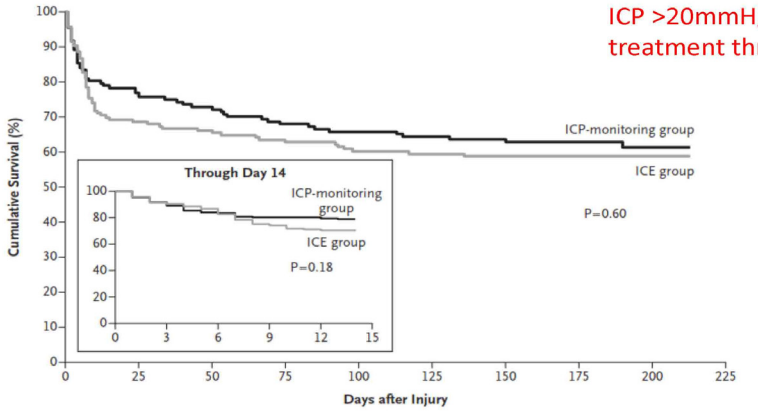


Dramatic ICP surge after 20mmHg
Old TBI trial used (ICP > 20mmHg) which showed a better clinical outcome.

Intracranial pressure: ICP > 20 mmHg ?

A Trial of Intracranial-Pressure Monitoring in Traumatic Brain Injury

N Engl J Med 2012;



ICP >20mmHg may not be a good treatment threshold for everyone.

2. Clinical signs and consequences

- **Signs and symptoms**
  - Headache, Nausea, Vomiting
  - Decreased consciousness, pupillary dilatation
  - Respiratory compromise (Chenyne-Stokes)
  - Cushing reflex : Bradycardia – ICP – BP elevation
- **Consequences**
  - Focal or global hypoperfusion: CPP = MAP – ICP
  - Mechanical destruction due to herniated brain structure

Global hypoperfusion

- CPP = MAP – ICP :
  - High ICP means low perfusion

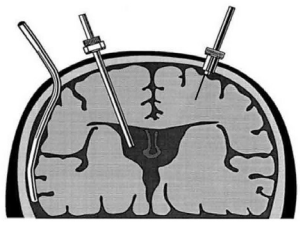
CASE illustration

Mechanical distortion/ disruption

- Herniation syndromes
  - Uncal
  - Downward central
  - Subfalcian
- Kernohan's notch phenomenon
- Duret hemorrhage

CASE illustration

ICP measurement

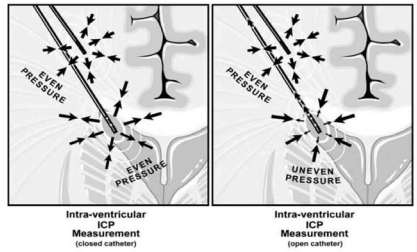


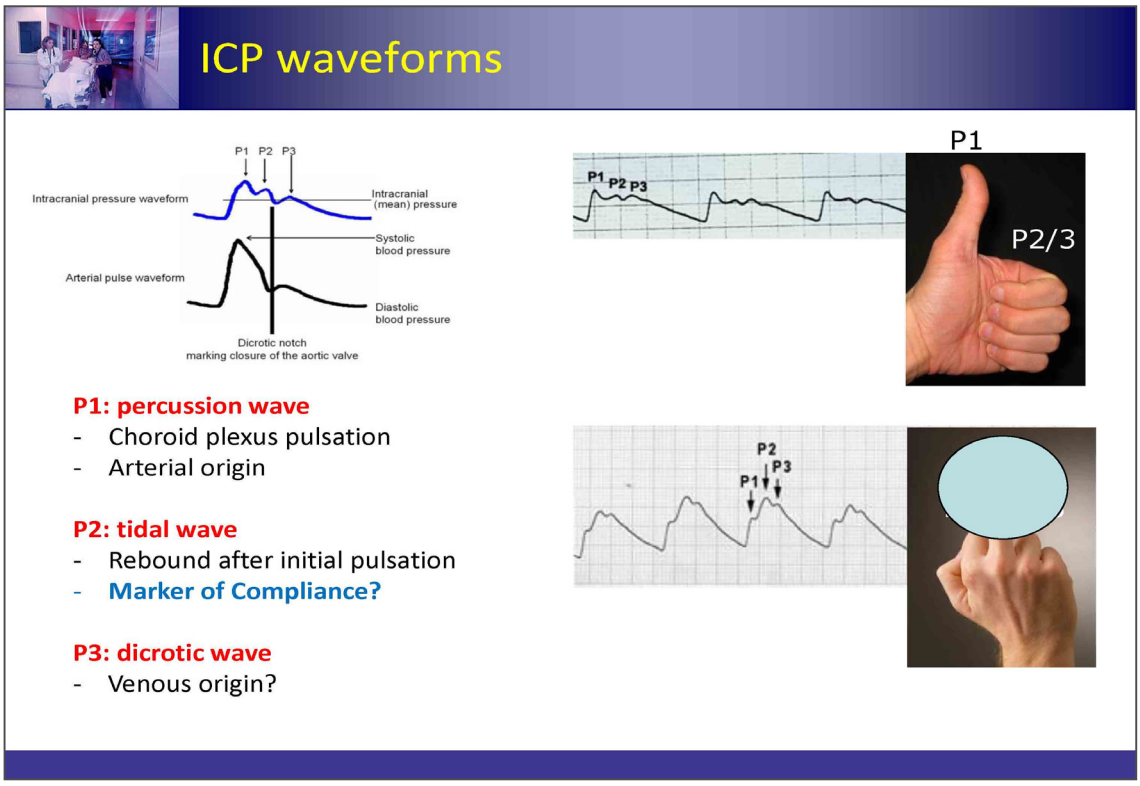
- EVD
  - Global ICP measurement
  - Re-zeroing is possible
  - Drain administration, blood drain
- Parenchymal probe
  - Focal ICP monitoring
  - Drift

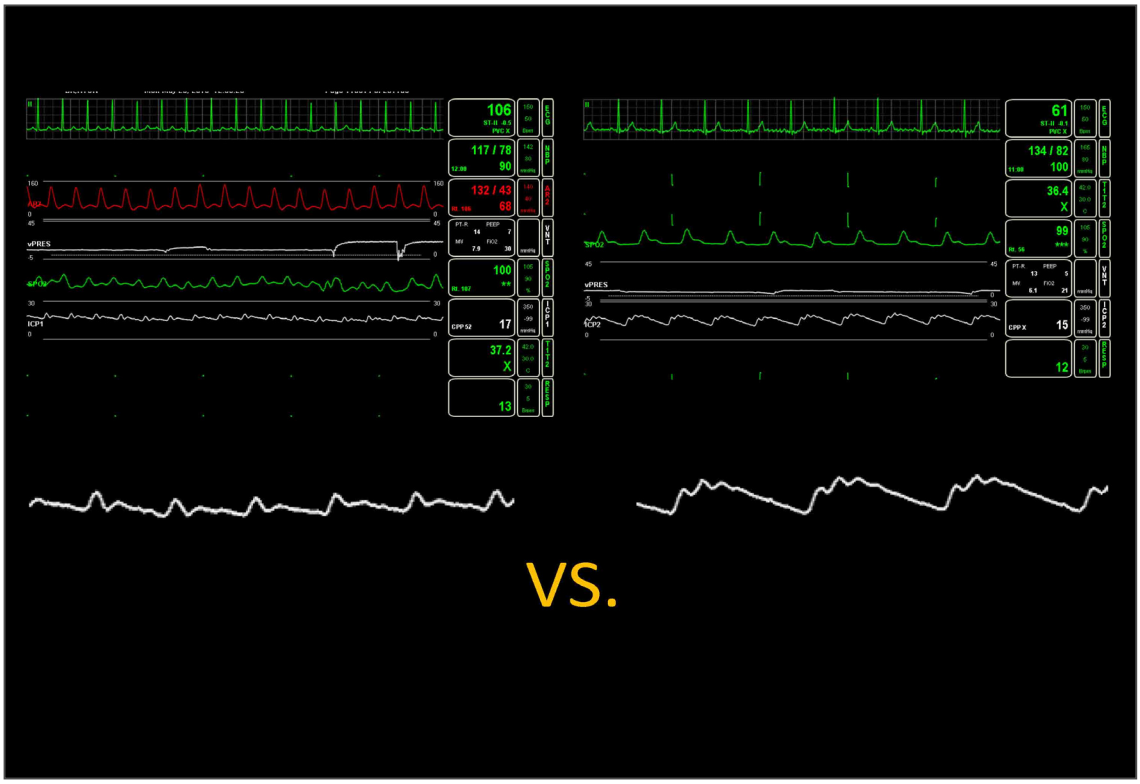
- Accuracy

Table 4. Paired t tests comparing the open and closed conditions for each monitor

Monitor	*df*	*t* statistic	*P* value
Parenchymal	9	−1.64	0.1357
Ventricular	9	−2.38	0.0414
Fluid-coupled	9	−2.63	0.0274



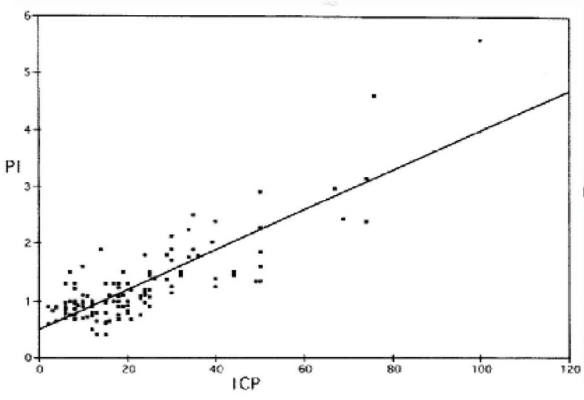

ICP waveforms
P1 P2 P3
Intracranial pressure waveform
Intracranial (mean) pressure
Systolic blood pressure
Arterial pulse waveform
Diastolic blood pressure
Dicrotic notch marking closure of the aortic valve
P1
P1 P2 P3
P2/3
P2
P1
P3
P1: percussion wave
- Choroid plexus pulsation
- Arterial origin
P2: tidal wave
- Rebound after initial pulsation
- Marker of Compliance?
P3: dicrotic wave
- Venous origin?

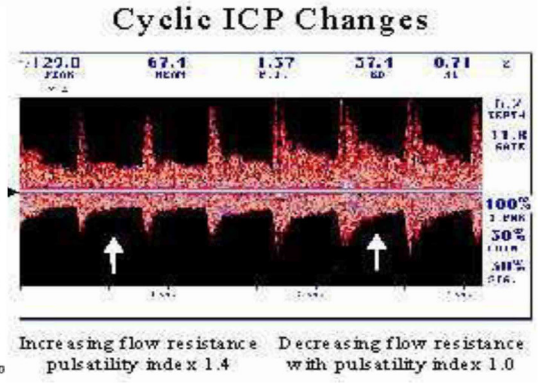

106
117 / 78
90
132 / 43
68
100
17
37.2
X
13
61
134 / 82
100
36.4
X
99
15
12
VS.

Non-invasive ICP

- Transcranial Doppler
  - Pulsatility index
    - Not affected by sono angle

$$P_i = \frac{V_s - V_d}{V_m}$$



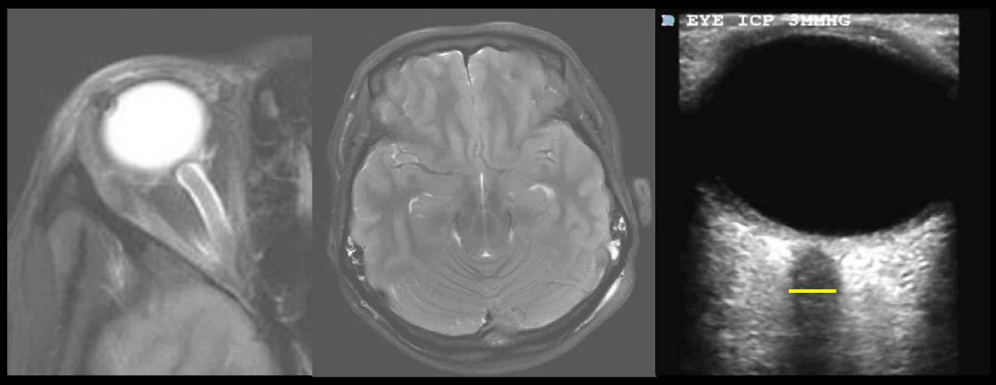


Increasing flow resistance pulsatility index 1.4

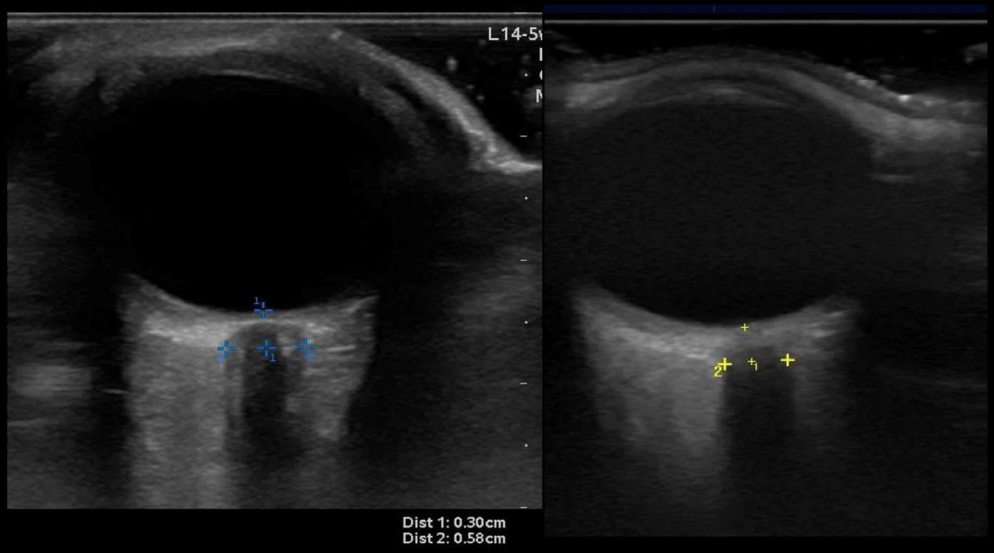
Decreasing flow resistance with pulsatility index 1.0

Non-invasive ICP measurement (3)

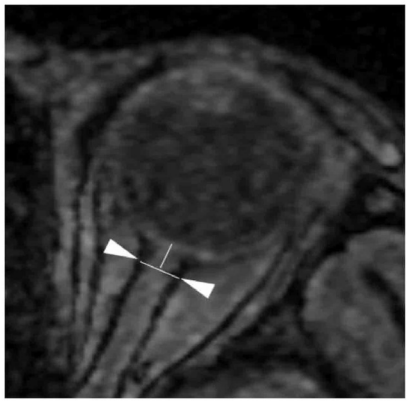
- More practical: B mode US

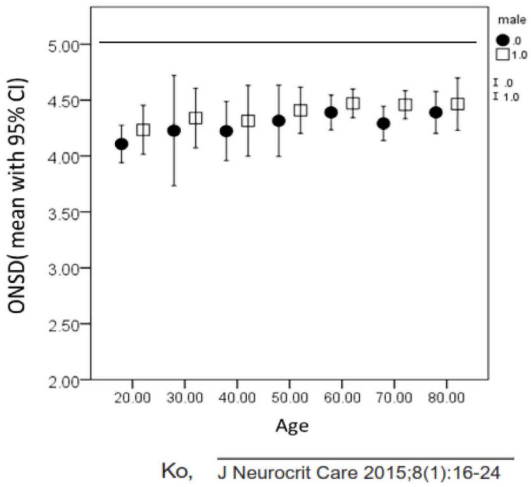


ONSD



ONSD : normal population





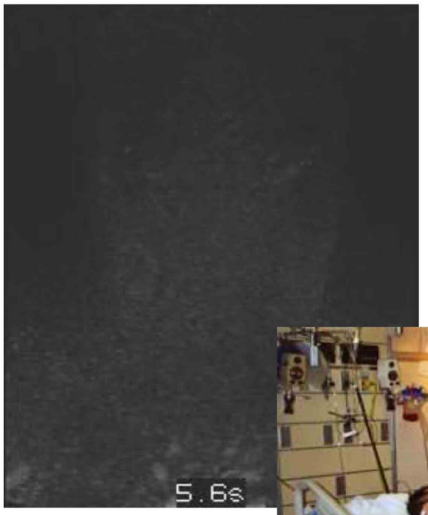
Ko, J Neurocrit Care 2015;8(1):16-24

Stepwise approach

Seoul National University NeuroICU protocol

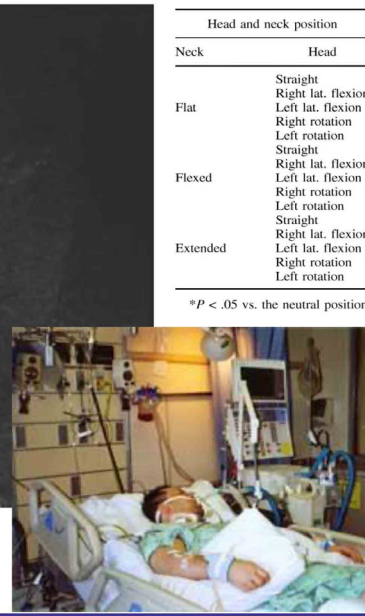
7. Pentobarbital /thiopental
6. Temperature management
5. Hyperventilation
4. Osmotic agent: Mannitol vs. HTS
3. CPP optimization: consider AR status
2. Proper sedation with short acting agent
1. Surgical Decompression : EVD

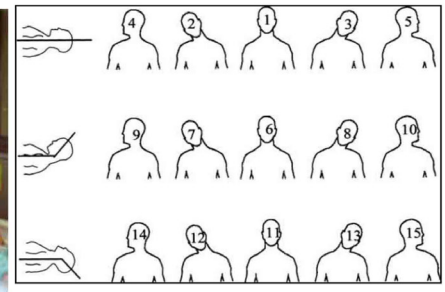
1. First basic thing: Neck position



Head and neck position		Position (Fig 1.)	Table horizontal 0°	Table head-up +30°	Table head-down −30°
Neck	Head				
	Straight	1	8.8 ± 2.5	7.0 ± 3.3	13.3 ± 2.9*
	Right lat. flexion	2	11.6 ± 4.3	10.0 ± 4.1	14.6 ± 5.1
Flat	Left lat. flexion	3	11.9 ± 4.3	10.4 ± 4.0	14.9 ± 5.9
	Right rotation	4	13.6 ± 4.6	12.5 ± 4.3	15.4 ± 3.6*
	Left rotation	5	12.9 ± 3.8	12.5 ± 3.3	16.2 ± 3.0*
	Straight	6	13.8 ± 4.7	12.2 ± 5.0	17.3 ± 5.7
	Right lat. flexion	7	14.7 ± 5.0	13.2 ± 5.0	18.2 ± 6.7
Flexed	Left lat. flexion	8	14.5 ± 5.1	13.1 ± 5.3	18.9 ± 6.9
	Right rotation	9	16.2 ± 3.9*	16.0 ± 3.2*	19.1 ± 3.8*
	Left rotation	10	15.8 ± 3.8*	15.4 ± 3.4*	19.2 ± 3.8*
	Straight	11	10.7 ± 4.0	9.4 ± 5.0	13.4 ± 4.9
	Right lat. flexion	12	12.0 ± 3.4	11.0 ± 4.5	14.4 ± 4.5
Extended	Left lat. flexion	13	11.5 ± 4.8	11.6 ± 5.3	14.1 ± 4.9
	Right rotation	14	12.8 ± 4.0	11.2 ± 4.8	15.6 ± 5.5
	Left rotation	15	13.2 ± 4.5	11.5 ± 5.9	15.3 ± 5.5

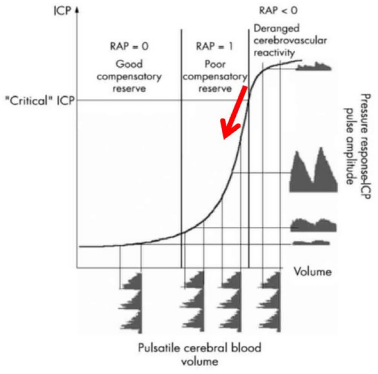
*$P < .05$ vs. the neutral position (1) with the table horizontal.

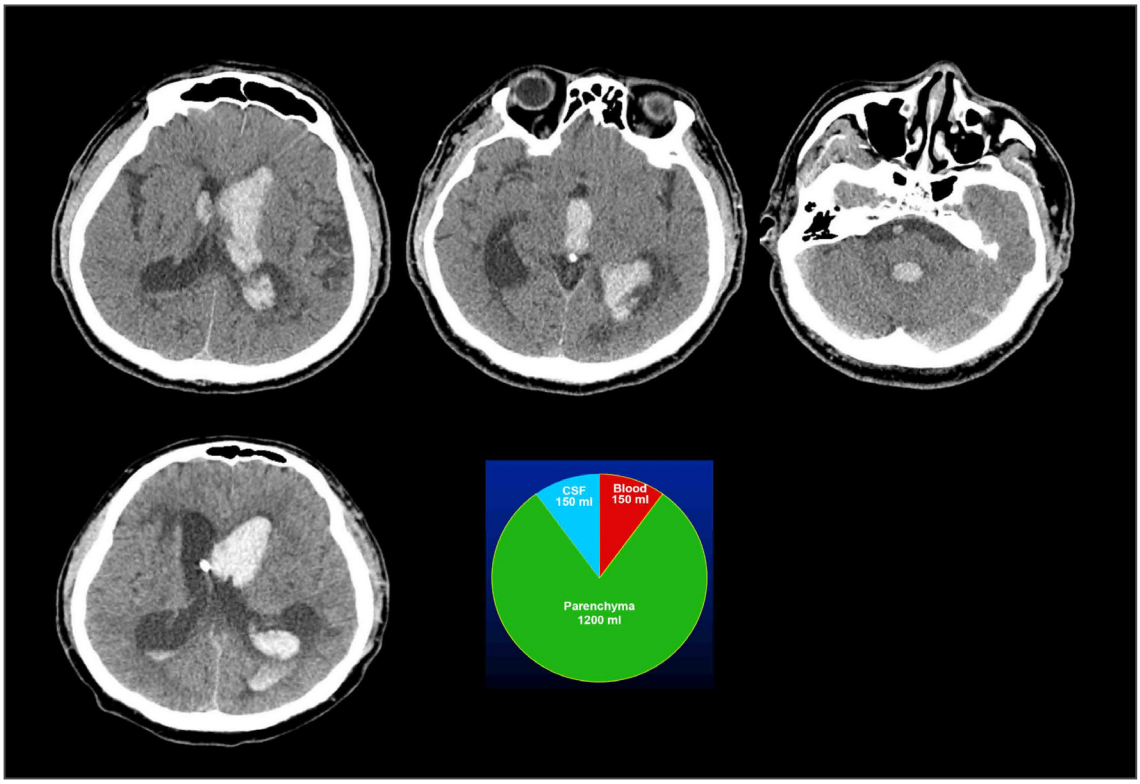




1. Surgical decompression: EVD

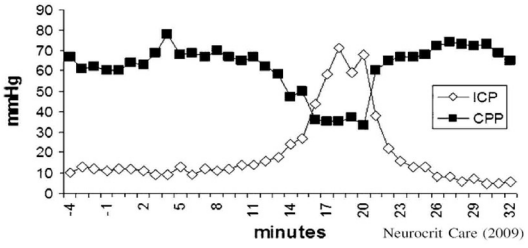
- Bedside EVD if indicated (hydrocephalus/ IVH)
- Double check whether drain is working
  - CSF oscillation / EVD clamped?
- Drain CSF a little bit
  - Decrease EVD level





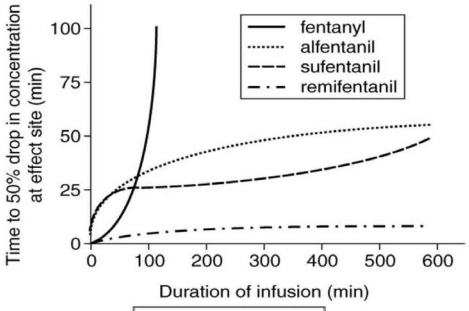
Step 2: proper sedation/analgesia

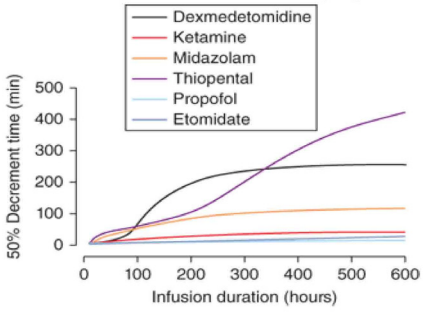
- Reversible sedation to allow repeated neuro-examination
- Drugs : Decrease brain metabolism -> decrease ICP
  - Remifentanil (Ultiva): 0.03 mcg/kg/min
  - Precedex : 0.3mcg/Kg/h –> dose titration
  - Midazolam : 0.05-0.2mg/Kg/h
  - Propofol : propofol infusion syndrome, infection, hypotension

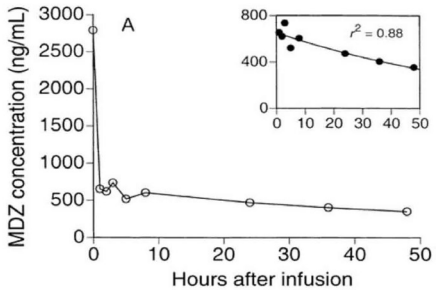


- Short acting agent
- For neuroexam, stop sedation and exam then restart sedation

Context sensitive half life prolongation

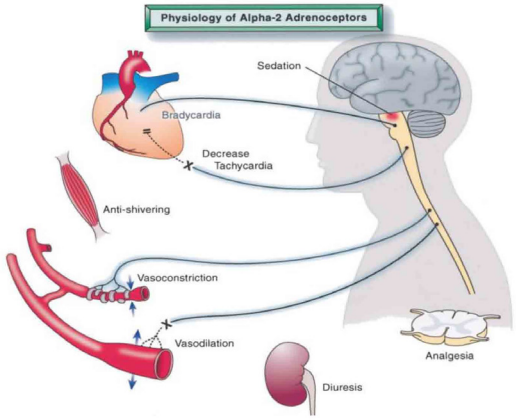






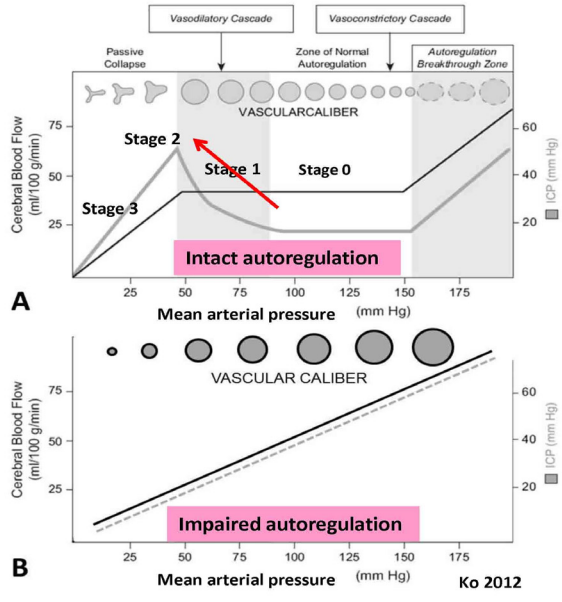
- RemiFTN: 3.8min
- Plasma and tissue esterase
- Liver / renal injury – no change
- 0.03mcg/kg/min ~

Precedex



Drug	$\alpha_2:\alpha_1$ Selectivity	dT ½	eT ½	Product Availability	Bioavailability	Protein Binding
Guanfacine	2,640	2.5 h	17 h	PO	~100%	70%
Dexmedetomidine	1,600	6 m	2 h	IV	70-80%	94%
Medetomidine	1,200					
Clonidine	220	11 m	13 h	PO TDS	100%PO 60%TDS	40%
methyldopa		12 m	105 m	PO/IV	50%	<20%
Guanabenz		60 m	6 h	PO	75%	90%

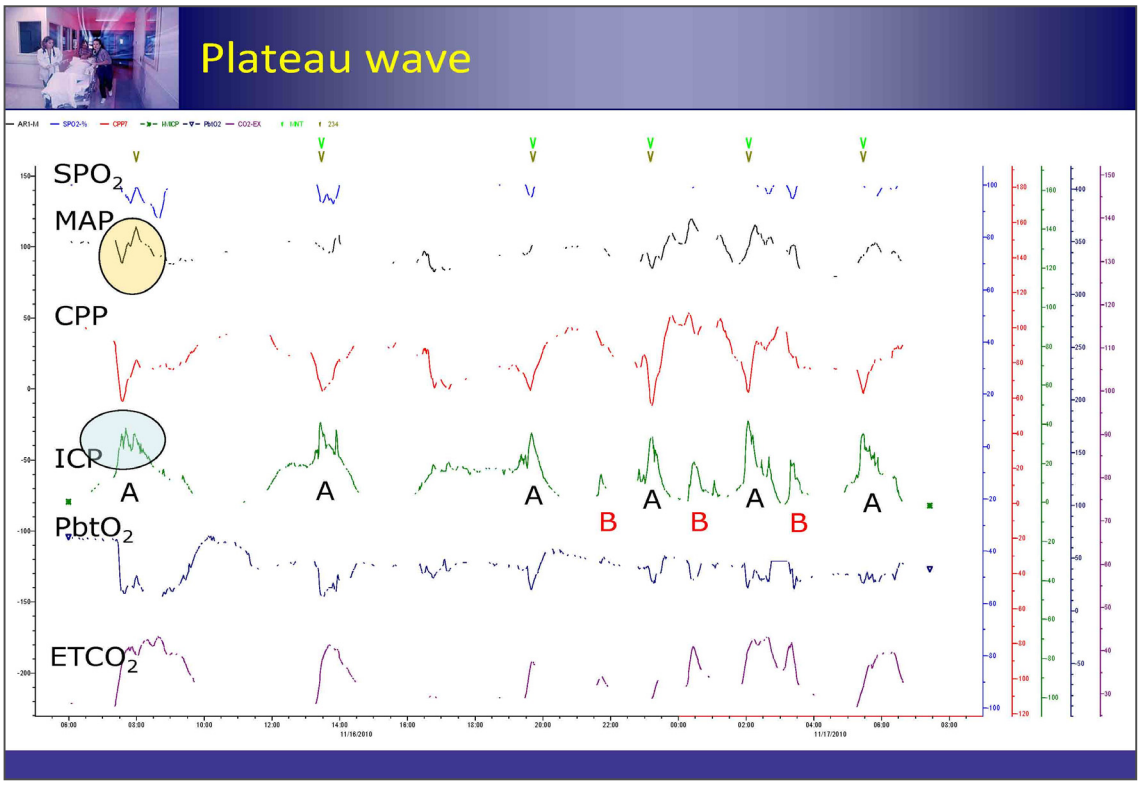
Step 3. CPP optimization

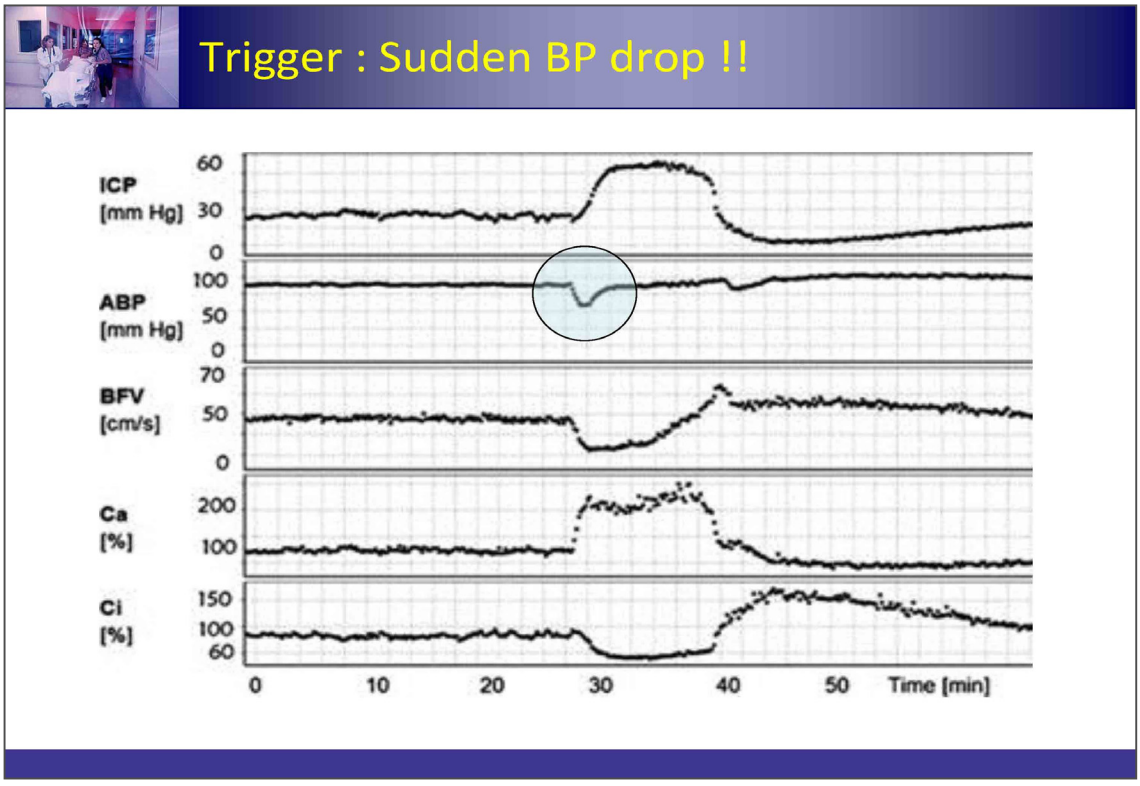


- BP: 100/60 mmHg (MAP – 70)
- ICP: **28** mmHg
- RR: 20, $ETCO_2$: 30
- Collapsed IVC

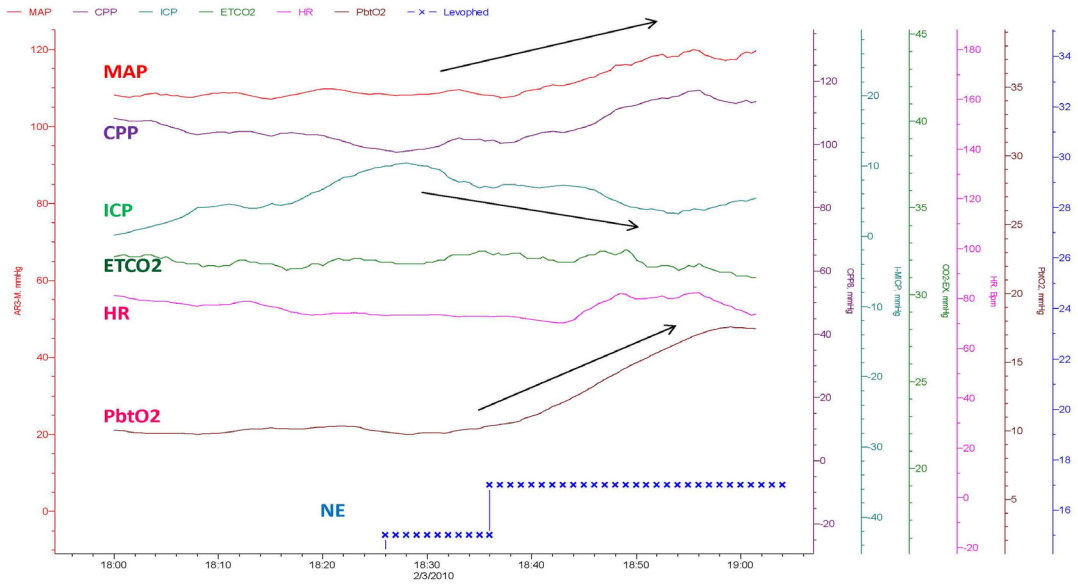
- Mannitol?

BIG NO NO

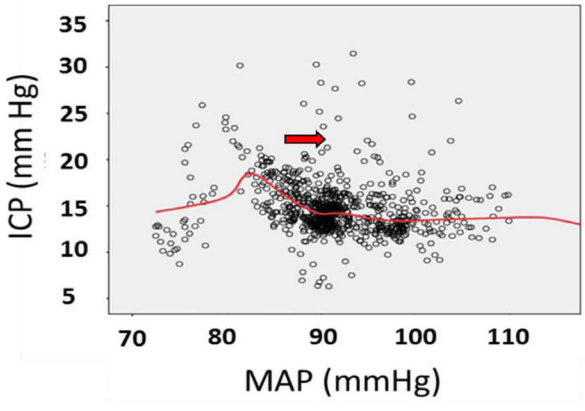

Plateau wave
SPO2
MAP
CPP
ICP
PbtO2
ETCO2
A
B

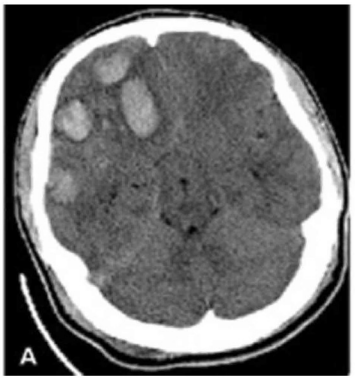

Trigger : Sudden BP drop !!
ICP
[mm Hg]
ABP
[mm Hg]
BFV
[cm/s]
Ca
[%]
Ci
[%]
Time [min]

CPP/MAP optimization



Step 3: CPP/MAP optimization





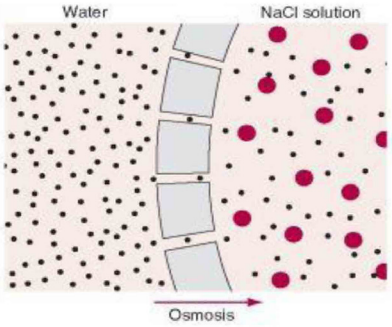
- ICP / MAP scatterplot -> intact cerebral autoregulation
- In cases with low CPP (MAP-ICP)< 50, MAP should be increased..

Step 4: Osmotic agents (1)

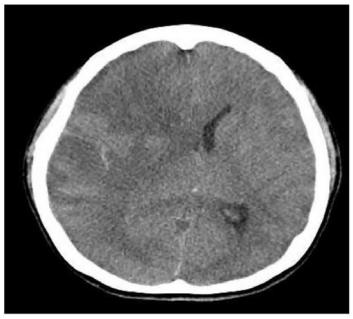
- **Mannitol:** 184KD sugar
  - Osmotic diuresis
  - Rapid onset: within minutes
  - Last up to 5 hrs (Peak 2hrs)
  - Form: **15% -25%** g/100ml

Table 1. Comparison of Osmotic Agents

Solution Concentration	Sodium Concentration (mEq/L)	Osmolarity (mOsm/L)
Ringer's lactate	130	275
0.009	154	308
0.02	242	684
0.03	513	1062
Mannitol 20%	n/a	1098
Mannitol 25%	n/a	1375
0.075	1283	2566
0.234	4004	8008



Step 4: Mannitol (2)



M/45, left side weakness, 180cm 80Kg
170/86 mmHg

20% Mannitol dose?

1) 50cc
2) 100cc
3) 150cc
4) 200cc

- Dosing: 0.5g/Kg – 1.5g/Kg (1g/Kg)
  - **< 0.5g/Kg** : little effect and unpredictable results
- *Less than 0.5g/kg of mannitol : controls ICP in 20%*
- *More than 0.5g/kg : controls ICP in more than 75%*

Step 4: Mannitol (2)

MAJOR CLINICAL AND PHYSIOLOGICAL BENEFITS OF EARLY HIGH DOSES OF MANNITOL FOR INTRAPARENCHYMAL TEMPORAL LOBE HEMORRHAGES WITH ABNORMAL PUPILLARY WIDENING: A RANDOMIZED TRIAL

TABLE 3. Early improvement of bilateral pupillary widening in the two groups of patients[a]

Pupillary improvement	No. of patients		
	HDM group	CDM group	Total
Yes	10	3	13
No	5	10	15

TABLE 4. Early improvement of unilateral pupillary widening in the two groups of patients[a]

Pupillary improvement	No. of patients		
	HDM group	CDM group	Total
Yes	44	29	73
No	13	27	40

Higher dose (1.4 g/kg) was more powerful than 0.7 g/kg in TBI RCT
Neurosurgery 2002

- Standard dose in USA – 1.0g/kg

Stopping point

- Direct Mannitol effect
  - Not merely due to hypersomolarity
    - Hypertonic saline: much fewer RF
    - Stopping s-osm >320: no evidence

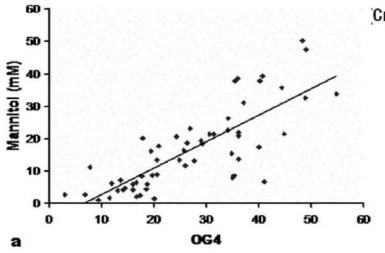
Osmolality and osmotic gap

Timing of Measurement	No MI-ARI*	MI-ARI*	p Value†
osmolality (mOsm/kg)			
baseline	301 ± 9	303 ± 4	0.556
before MI-ARI	320 ± 22	322 ± 23	0.481
peak	320 ± 22	344 ± 25	0.025

  - Acute tubular necrosis
  - Pre-renal type injury
    - Euvolemia: mandatory

Step 4: Mannitol (3)

- **Osmolar gap** : Measured osm – Calculated osm
  - Well correlated with Mannitol concentration



Crit Care Med 2004;

Osm: 2Na + BUN/2.8 + Glu/18

  - **OG > 55 mOsm**
    - Retrospective analysis:
      - Mannitol induced RF (+): OG > 65 mOsm
      - Mannitol induced RF (-): OG < 55 mOSm

Mannitol order

- **Patients with ICP monitor**
  - 20% mannitol (XX)cc ivs (0.5-1g/Kg) (prn or q6h)
  - Check e', osm, BUN, glucose before next dose (OG calculation)
  - Routine N/S replacement (X)
  - Maintain euvolemia (I/O q 8h-6h)

- **Patients without ICP monitor**
  - 20% mannitol (XX)cc ivs (0.5-1g/Kg) (q6h-8h)
  - Check e', osm, BUN, glucose before next dose (OG calculation)
  - Routine N/S replacement (X)
  - Maintain euvolemia (I/O q 8h-6h)

Step 4: Hypertonic saline (1)

- HTS: 3% - 23.4% : A magic bullet
  - 0.9% Normal saline : **308 mEq/L**
  - Dose: **23.4% - 30cc** or equivalent amount of osmolarity
  - Korea : 11.7% **NACL4IP** : 40mEq/20cc - 60cc IV shooting

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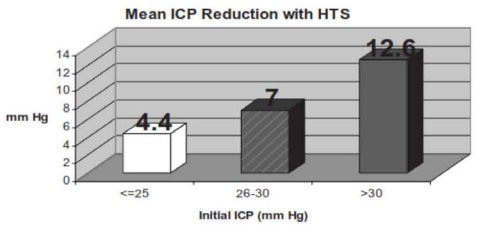
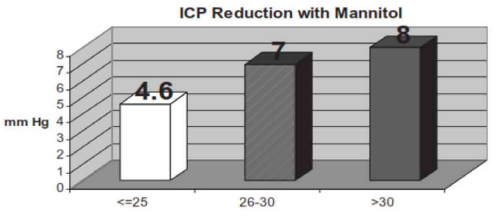
The Use of 23.4% Hypertonic Saline for the Management of Elevated Intracranial Pressure in Patients With Severe Traumatic Brain Injury: A Pilot Study

(*J Trauma.* 2009;67: 277–282)





HTS and Blood pressure

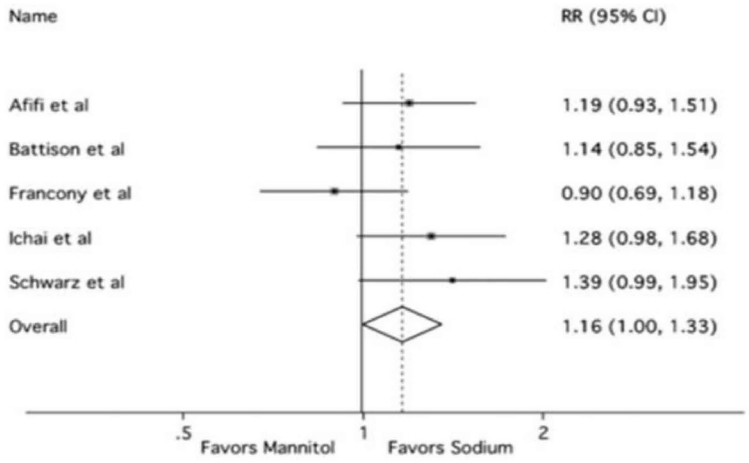
Table 1. Systemic Responses to Rapid Hypertonic Saline Infusion

		Time after HTS administration	
	Baseline	45 s	5 min
HR (beats/min)	101 ± 8	103 ± 6	114 ± 9[a]
MAP (mm Hg)	95 ± 4	51 ± 5[a]	113 ± 8[a,b]
PP (mm Hg)	36 ± 3	48 ± 4[a]	47 ± 4[a]
MPAP (mm Hg)	14 ± 1	17 ± 1[a]	15 ± 1
CO (L/min)	2.8 ± 1.0	3.9 ± 1.1[a]	4.0 ± 0.9[a]
SV (mL)	26.4 ± 1.5	38.5 ± 1.9[a]	34.3 ± 2.1[a]
SVR (dynes·s·cm^{-5})	2628 ± 220	1069 ± 159[a]	2071 ± 367[a,b]
PVR (dynes·s·cm^{-5})	261 ± 18	187 ± 16[a]	174 ± 23[a]

- Slow infusion via central line over 10min
  - Peripheral line: phlebitis

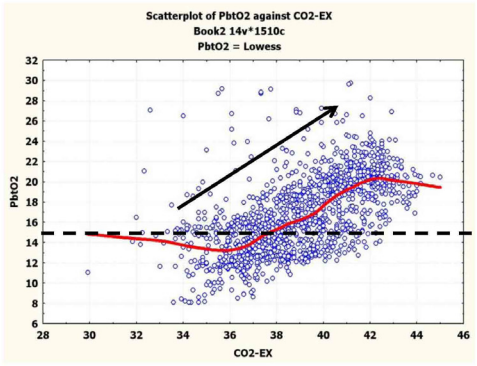
HTS vs Mannitol

Hypertonic saline versus mannitol for the treatment of elevated intracranial pressure: A meta-analysis of randomized clinical trials*



Step 5: Hyperventilation

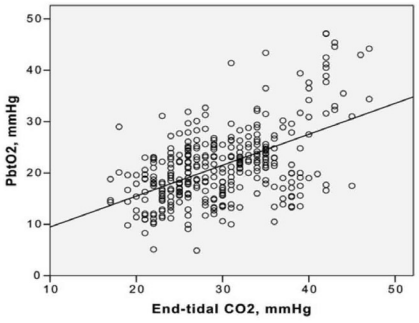
- Decrease $PaCO_2$ -> Vasoconstriction -> decrease CBV -> ICP ↓
- Side effect : brain hypoxia, **even PaCO2 around 30 mm Hg**
  - Fixed degree of hyperventilation without brain oxygen monitoring can be harmful



Patient with ICH

Spontaneous hyperventilation and brain tissue hypoxia in patients with severe brain injury

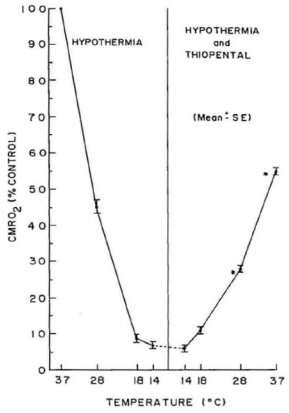
Emmanuel Carrera,[1] J Michael Schmidt,[1] Luis Fernandez,[1] Pedro Kurtz,[1] Maxwell Merkow,[2] Morgan Stuart,[2] Kiwon Lee,[1,2] Jan Claassen,[1,2] E Sander Connolly,[2] Stephan A Mayer,[1,2] Neeraj Badjatia[1,2]



J Neurol Neurosurg Psychiatry 2010;**81**:793–797.

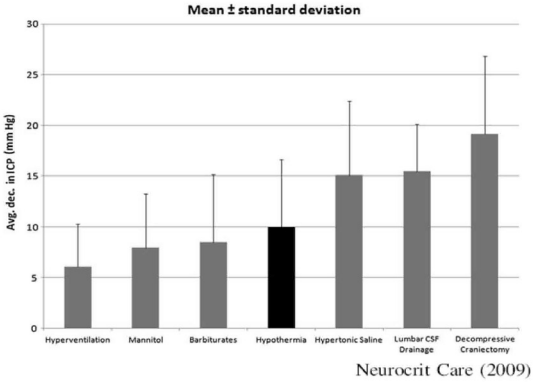
Hypothermia: Mechanism of ICP control

- Mechanism
  - Decreases metabolism
  - Coupled decrease in CBF



6% / 1°C

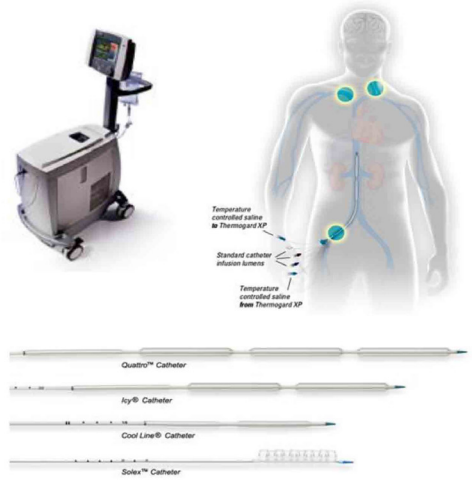
- Target temperature
  - For ICP: < 35



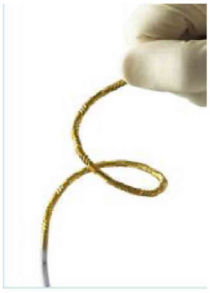
Neurocrit Care (2009)

Intravascular Cooling

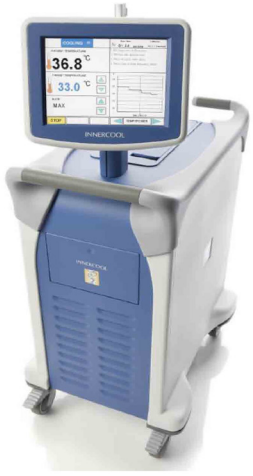
- **Alsius (ZOLL): Medipia Korea**



- **Philips INNERCOOL**



ACCUTROL

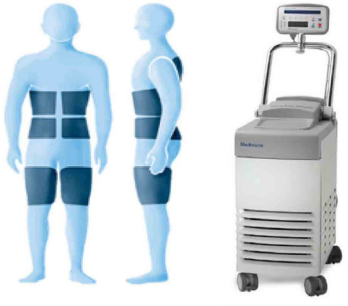


High surface area for cooling
Thrombogenic, DVT : ICTuS-L

Surface cooling

- **Arctic Sun (Medivance)**

Pavmed (Korea)

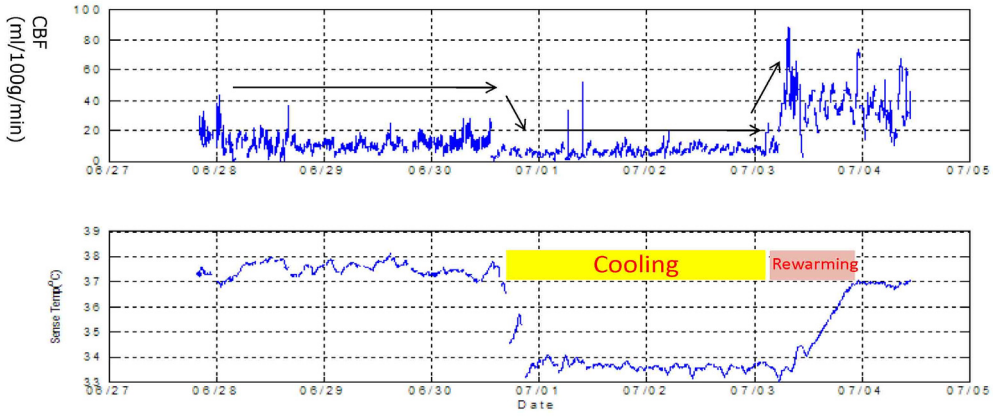


Covers 40% of BSA

- **Innercool STx surface**

No adhesive
Less skin irritation
No direct data yet

Hypothermia and CBF

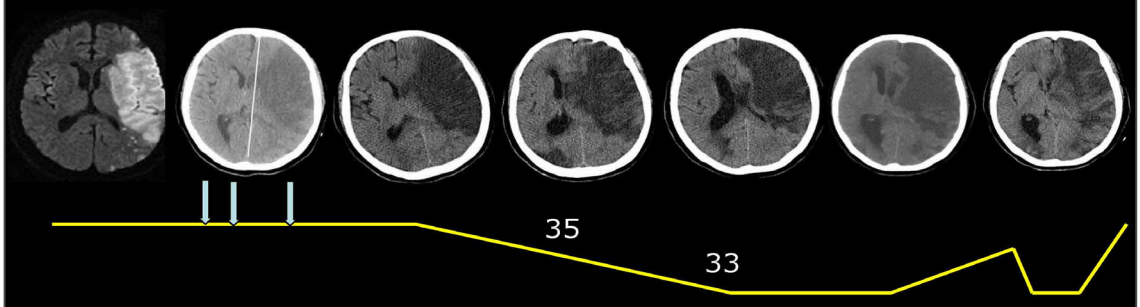


***Ko et al**. 2010*
NY Conference of
Neurologic Emergency

Cooling decreases CBF (ICP decrease)
Rewarming -> rebound ICP/CBF increase

Malignant MCA case: simple

Malignant MCA case: complex



TTM decreases or may halt brain edema/swelling

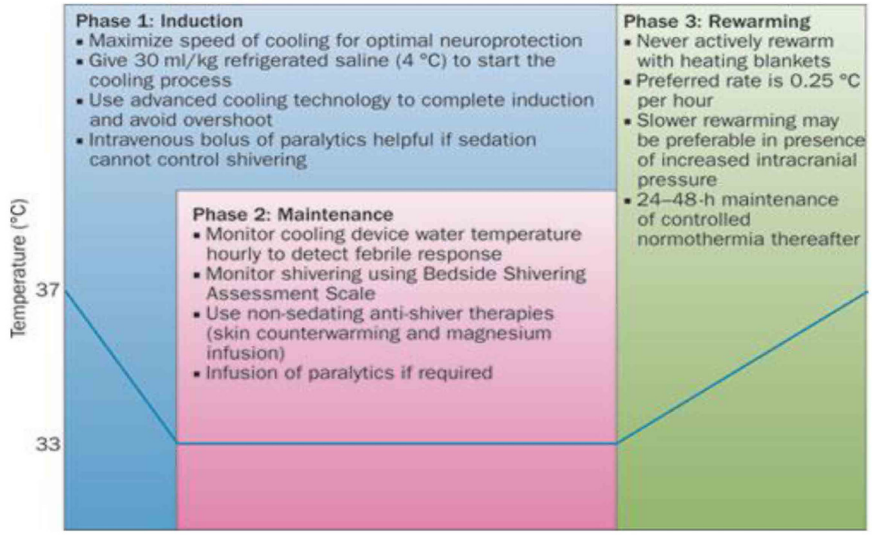
Rewarming induce rebound edema/swelling

TTM may translate into better neurologic outcome

Difference

	Cardiac arrest	ICP modulation
Target	32-34 or 36	From 35.5 -> 33 Dose dependent
Duration	24hours	Variable More than 3-4 days
Rewarming	Fixed rate At 0.25C /hour	Variable 0.05C/hour
Adjustment	Not needed	Rebound edema Re-cooling

Phases of cooling

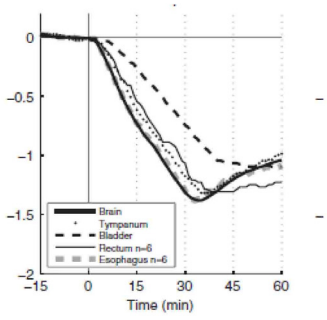


Insulin resistance
Cold diuresis
K influx

Opposite of cooling
K efflux – VT/Vf

Temperature monitoring site

- Where to monitor patient's temperature
  - Gold standard: pulmonary artery
  - Skin (axillary): xxxxx
  - Esophagus
  - Bladder
  - Rectal



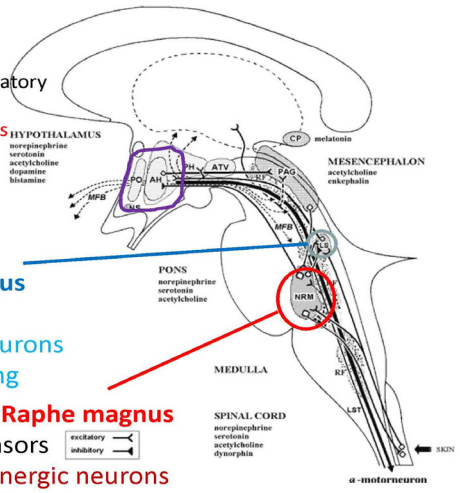
Bladder : Time lagging in fast cooling

Urine output dependent

Maintenance -> no problem in all 3 probes

Thermoregulation

Main thermoregulatory center:
Ant. Hypothalamus



Locus subcoeruleus
Cold sensors
Noradrenergic neurons
Promotes shivering

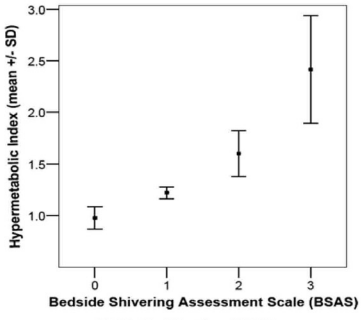
Nucleus Raphe magnus
Heat sensors
Serotoninergic neurons
Inhibits shivering

Serotonin -> Antishivering
NE blocker -> Antishivering

Shivering

- BSAS

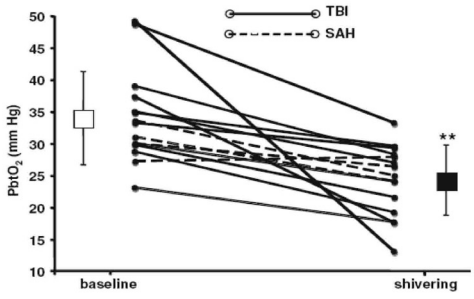
Score	Definition
0	**None:** no shivering noted on palpation of the masseter, neck, or chest wall
1	**Mild:** shivering localized to the neck and/or thorax only
2	**Moderate:** shivering involves gross movement of the upper extremities (in addition to neck and thorax)
3	**Severe:** shivering involves gross movements of the trunk and upper and lower extremities



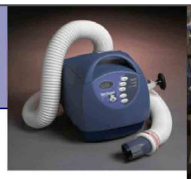
Badjatia *Stroke*. 2008

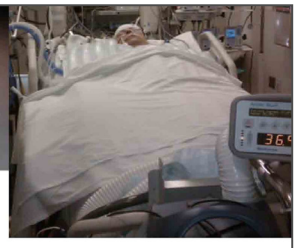
Effect of Shivering on Brain Tissue Oxygenation During Induced Normothermia in Patients With Severe Brain Injury

Mauro Oddo · Suzanne Frangos · Eileen Maloney-Wilensky · W. Andrew Kofke · Peter D. Le Roux · Joshua M. Levine



Anti-shivering protocol





Prevention of Shivering During Therapeutic Temperature Modulation: The Columbia Anti-Shivering Protocol

Choi and Ko et al. *Neurocrit Care*

Step		Intervention	Dose
0	Baseline	Acetaminophen	650–1000 mg Q 4–6 h
		Buspirone	30 mg Q 8 h
		Magnesium sulfate	0.5–1 mg/h IV Goal (3–4 mg/dl)
		Skin counterwarming	43°C/MAX Temp
1	Mild sedation	Dexmedetomidine	0.2–1.5 mcg/kg/h
		or	Fentanyl starting dose 25 mcg/h
		Opioid	Meperidine 50–100 mg IM or IV
2	Moderate sedation	Dexmedetomidine and Opioid	Doses as above
3	Deep sedation	Propofol	50–75 mcg/kg/min
4	Neuromuscular blockade	Vecuronium	0.1 mg/kg IV

90%

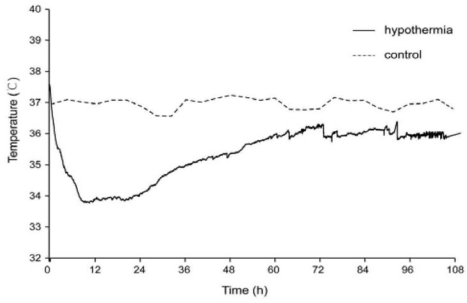
Malignant MCA - TTM

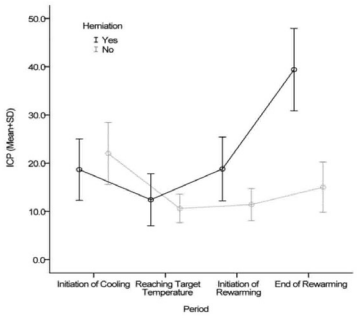
Improved Neurological Outcome With Mild Hypothermia in Surviving Patients With Massive Cerebral Hemispheric Infarction (*Stroke*. 2016;47:457-463.

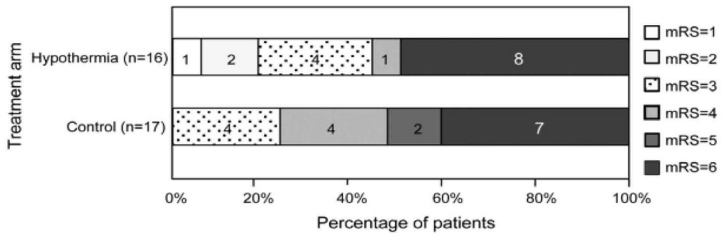
Table 1. Patient Characteristics

	Hypothermia Group (n=16)	Control Group (n=17)	*P* Value
Age, y (range)	59.8±8.6 (46–75)	68.5±8.5 (53–79)	0.006
Gender, male/female	15/1	10/7	0.039
Underlying disease			
Hypertension	11	13	0.708
Coronary heart disease	3	5	0.688
Atrial fibrillation	5	7	0.721
Hyperlipidemia	5	2	0.225
Valvular dysfunction	1	2	1.000
Diabetes mellitus	3	6	0.438
Stroke	4	4	1.000
Affected hemisphere, left/right	11/5	11/6	1.000
Infarcted area, 2/3 MCA/MCA/>MCA	5/8/3	4/9/4	0.868
Mean GCS (range)	9.8±2.2 (7–14)	9.2±2.2 (7–14)	0.468
Mean NIHSS (range)	19.7±2.9 (15–25)	20.4±3.8 (15–25)	0.541
Mean APACHE II (range)	13.3±4.0 (8–20)	14.5±4.7 (7–22)	0.433
Transtentorial herniation	1	3	0.601
Prior T/A/A/D	7	8	1.000

Cooling for edema

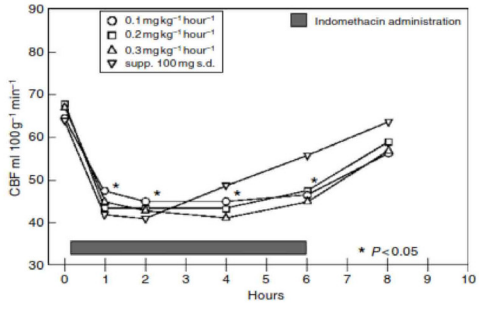


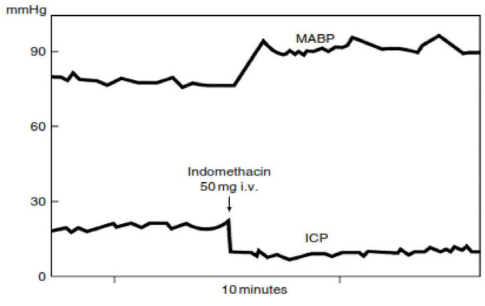




Rescue therapy etc.

- Vasoconstrictor : indomethacin





Iv = 0.1-0.4mg/kg (한국 iv 제제 없음)
p.o; 100mg oral
P.R = 100mg suppository

Pentobarbital coma therapy

- Rarely used due to toxicity..
- Should be on more than several days…
- Cardiac toxicity
- Renal toxicity
- Metabolic acidosis : prophylen glycol

Take Home messages

- Consider surgical simple decompression
  - EVD status
  - Check whether drain is working
- Control agitation
- Optimize hemodynamic status
- Consider Osmotic agent; mannitol : 0.5g/kg
  - Osmolar Gap
  - HTS is more potent
- Transient hyperventilation
- Therapeutic temperature modulation if needed